INTERFERON-MEDIATED LONG NON-CODING RNA RESPONSE IN MACROPHAGES IN THE CONTEXT OF HIV

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Interferons play a critical role in the innate immune response against a variety of pathogens, such as HIV-1. Recent studies have shown that long non-coding genes are part of a reciprocal feedforward/feedback relationship with interferon expression. They presumably contribute to the cell type specificity of the interferon response, such as the phenotypic and functional transition of macrophages throughout the immune response. However, no comprehensive understanding exists today about the IFN-lncRNA interplay in macrophages, cells that also serve as a sanctuary for latent HIV-1. Therefore, we completed a poly-A+ RNAseq analysis on monocyte-derived macrophages (MDMs) treated with members of all three types of IFNs (IFN-α, IFN-ε, IFN-γ or IFN-λ) and on macrophages infected with HIV-1, revealing an extensive non-coding IFN and/or HIV-1 response. We focused on the long non-coding fraction of the transcriptome: a total of 1082 discovered unique differentially expressed non-coding genes over all four IFN conditions were identified. HIV infection caused 116 non-coding genes to be differentially expressed. Furthermore, using a co-expression correlation analysis (WGCNA), we identified a cluster of genes that are highly enriched for genes involved in the interferon and/or anti-viral response. Based on predicted ncRNA-mRNA interactions and genomic co-localization, important (long) non-coding hub genes within this IFN- or HIV-1-associated networks were identified, including TNK2-AS1, FIRRE, DANCR, RP3-47704.14, AC064834.3 and NRIR. This study identified and prioritized IFN and HIV infection related hub lncRNAs for further functional validation.